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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
04/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/584,449	PAI ET AL.	
	Examiner	Art Unit	
	SATYANARAYANA R. GUDIBANDE	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9-11 and 14-23* is/are pending in the application.

4a) Of the above claim(s) *5 and 20-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,9-11 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/19/09 has been entered.

Priority

Applicant's claim for the benefit of a prior-filed foreign application under 35 U.S.C. 119(a-d) is acknowledged, i.e., foreign priority document has been placed in the application file. However, applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(a-d) as follows:

Although, the Bib data sheet indicates that the requirement for granting foreign priority has been satisfied with the certified foreign priority document placed in the application, the filing date of the priority document has not been perfected. The foreign priority document submitted is not in English language. A translation of the same is required to grant the priority. The filing date of the priority document is not perfected unless applicant has filed a certified priority document in the application (and an English language translation, if the document is not in English) (see 37 CFR 1.55(a)(3)).

Specification

1. The disclosure is objected to because of the following informalities:

The **subheadings** for the various experiments presented in the specification on pages 21-35 are not clear. For example, examples have been divided into Comparative examples (1-5), Examples (1a-7) and Experiments (1-4).

Especially, for e.g., **Experiment 3: Evaluation 1 of efficacy for animals** (page 3)

It would be appropriate if it read **Experiment 3: Evaluation composition 1 for efficacy in animals.**

Appropriate correction is required.

2. The use of symbol "~" to recite range of in ratios of different ingredients (components) on pages 10 (lines 5-8), 11 (line20), 13 (lines 5 and 6), 16 (line 20) and elsewhere in the document needs to be replaced with hyphen "-".

3. The lengthy specification (37 pages) has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

4. The specification of the instant application also lacks the required format for presentation as provided in 37 CFR 1.77(b). The instant specification does not conform to the guidelines with sections under different titles such as:

(b) Cross-reference to related applications,

(f) Background of the invention.

(1) Field of the invention.

(2) Description of related art including information disclosed under 37 CFR 1.97 and 1.98.

(g) Brief summary of the invention, etc.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Election/Restrictions

Applicant's amendment to claims in the response filed on 1/26/09 has been acknowledged.

Applicant's election with traverse of group I (claims 1-19) and election of species in the following table,

No.	Species	Election
1.	1-5, 9, 10, 20 & 22 Water-soluble drug	Insulin
2.	1, 6, 7, 9, 10 & 20 Counter-ion substance	Sodium salt of C8-C18 fatty acid
3.	1, 11, 12 & 20 Lipid	monoglyceride
4.	1, 13 & 20 Polymer	Methacrylic acid copolymer
5.	17 & 18 Cryoprotecting agent	mannitol
6.	1, 14, & 20 Emulsifier	Polyoxyethylene polyoxypropylene copolymer
7.	22 pH adjusting agent	Citric acid

in the reply filed on 2/27/08 was acknowledged and the traversal arguments were answered in the office action dated 4/23/08.

Status of pending claims

Claims 1-5, 7, 9-11 and 14-23 are pending.

Claim 5 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/27/08.

Art was found on the elected species of insulin and has been applied in the rejections below. Hence claim 5 which is drawn to drug that is other than the elected species insulin has been withdrawn from further consideration.

Claims 20-23 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking

claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/7/08.

Claims 6, 8, 12 and 13 have been canceled.

Claims 1-4, 7, 9-11 and 14-19 are examined on the merit.

Any objections and/or rejections made in the office action dated 11/26/08 and not specifically discussed in original and/or modified form here are considered withdrawn.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

Applicant's arguments, see page 6-7, filed 1/26/09, with respect to claims 1-3, 9-11, 15 and 17 have been fully considered and are persuasive. The written description rejection of claims 1-3, 9-11, 15 and 17 has been withdrawn.

Claim Rejections - 35 USC § 102(b)

Applicant's arguments, see page 7-8, filed 1/26/09, with respect to claims 1, 2, 7, 11-15, and 17-19 have been fully considered and are persuasive. The anticipation rejection of claims 1, 2, 7, 11-15, and 17-19 has been withdrawn.

Claim Rejections - 35 USC § 103

Applicant's arguments, see page 8, filed 1/26/09, with respect to the rejection(s) of claim(s) 1-4, 7 and 9-19 under obviousness have been fully considered and are persuasive.

Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of applicant's amendments to claim 1.

New grounds of rejection

Claim Objections

1. Claim 1 is objected to because of the following informalities: On line 2, the punctuation "**:**" is missing after the transitional phrase "comprising". Appropriate correction is required.

2. Claim 1 recites the dimension of nanoparticle as less than 500 nm. However, the definition of the nanoparticle according to the Class 977 and subclass 773, the particle size should be 100 nm or less.

CLASS 977, NANOTECHNOLOGY

773**. Nanoparticle (structure having three dimensions of 100 nm or less):**
This subclass is indented under subclass 700. Subject matter wherein all three of the nanostructure's physical dimensions are of 100 nm or less.

3. The claim 15 recites a limitation "50% or less" for solubilizing agent. There is no lower limit recited for the concentration. The claim could be modified to recite "less than 50%" for clarity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

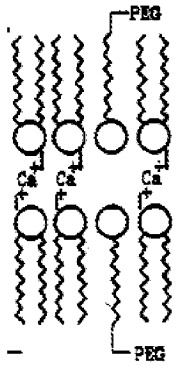
> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7, 9-11and 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (US 2003/0054027) in view of Rosenberger (US 2005/0170004).

In the instant application, applicants claim an orally administrable composition comprising: a complex of a charged water-soluble drug and a counter ion substance is an anionic or a cationic compound and depends on ionic nature of the water-soluble drug molecule, a lipid, a polymer and an emulsifier wherein the said complex is entrapped in said lipid and said polymer is inserted between said lipid.

Unger discloses a composition comprising a cochleate vesicle for delivery of bioactive agents comprising a charged lipid, a counter ion, a lipid covalently bonded to a polymer and the vesicles is <200 nm in size (claim 1 of Unger). A schematic diagram of the vesicle of Unger is shown below.



Unger discloses that the water soluble bioactive agent can be insulin (instant elected species) [0188]. Unger discloses saturated fatty acid such as palmitic acid (a C_{18} carboxylic acid) and oleic acid as a charged lipid that reads on the instantly elected counter ion [0056]. Unger also discloses that the charged lipid (palmitic acid), which is the counter ion and is present in the range 10-90 mole %. Since the counter ion is used in the neutralizing the charge on the water-soluble bioactive agent, the mole % of the complex will be in the range 10-90 mole %. This reads on the instant claims 1, 4, 7, 9 and 10. Unger discloses lipids such as glyceryl mono stearate (reads on the instantly elected monoglyceride), mono and diglycerides [0164] as lipids and that reads on instant claim 1. Unger discloses polymers such as methacrylates, polyhydroxy alkyl(meth)acrylates, etc and copolymers thereof ([0112] and claim 5 of Unger). Unger further discloses that the ratio of lipid to polymer is in the range 1-50 mole % and preferably 1-25 mole % that reads on the instant claims 1 and 11. Unger discloses use of mannitol as a polymer [0163] that is an elected species for the cryoprotecting agent used in the instant invention. This reads on instant claims 17 and 18. Unger discloses poloxamer 188, 184 and 181 that are polyoxyethylene and polyoxypropylene copolymers (reads on the instant elected species of emulsifier) [0164]. This reads on the instant claims 1 and 14. Unger discloses several solubilizing agents such as oleyl alcohol, propylene glycol [0164] that reads on the instant claims 15 and 16. The claim as

recited depicts a picture (no diagrams have been shown in the specification) that the complex of the drug and counter ion resides in a lipid vesicle that is surrounded by the polymer that penetrates the lipid layer. Unger discloses such a nanostructure in a schematic diagram as shown above. It is clear from the diagram shown that the (ionically) neutralized drug complex which is water soluble would reside in the lipid bilayer and the polymer shown incorporating into the bilayer provides stability to the structure. One of ordinary skill in the art would expect that that majority of water soluble ionic complex would reside in the lipid bilayer and hence more than 70% of the complex is entrapped in the nanoparticle or structure that surrounds itself with a polymer as shown in the diagram of Unger. This reads on the instant claims 1 and 2.

Unger does not explicitly teaches or discloses that more than 80% of the charged water soluble drug is retained in the nanoparticle when the composition is mixed with pancreatin as recited in instant claim 3.

Rosenberger studied the stability of glatiramer acetate (GA), a water soluble positively charged protein in nanoparticle in the presence of pancreatin ([0061], [0062], [0089] and table 1 on page 8). Pancreatin is a mixture of pancreatic proteases containing trypsin and chymotrypsin [0089]. Rosenberger's study as illustrated in table 1, clearly shows % of GA was stable with 80% intact in nanoparticle when treated with pancreatin even after 6 minutes. This reads on the instant claim 3.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Unger and Rosenberger to arrive at the instant invention. Unger discloses composition of nanoparticles wherein the charged drug complex entrapped nanoparticle composed of lipid and polymer as illustrated above and Rosenberger teaches that the GA entrapped in the nanoparticle

is stable in the presence of pancreatin. Both Unger and Rosenberger teaches the oral delivery of peptide drugs and Rosenberger clearly discloses the problems associated with oral delivery of peptide drugs considering the fact that the peptide is acted upon by the enzymatic systems of gastrointestinal tracts (GI) [0003]. Hence one of ordinary skill in the art would be motivated to incorporate the drug into a nanoparticle that would protect the water soluble peptide drug of the instant invention, insulin. One of ordinary skill in the art would test such a composition of insulin for stability in the presence of pancreatin as shown by Rosenberger in the case of glatiramer acetate. Unger teaches the ratios of lipids, polymers, etc., in mole % ratios instead of weight % as in the instant application. With regards to optimization of ranges, MPEP section 2144.05 states that "[G]enerally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Also, MPEP further states that, it is "[T]he normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable

expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654